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INFLUENZA STUDIES

IV. EFFECT OF VACCINATION AGAINST INFLUENZA AND SOME OTHER RESPIRATORY INFECTIONS *

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In this study approximately 6,000 persons were under observation from November, 1919, to June 1, 1920. About one half of these were vaccinated with the bacterial suspension to be described presently; the other half were not vaccinated; both groups lived as far as might be under identical conditions.

Three schools and two large hospitals for mental diseases were available for these observations. The general physical condition of the subjects was good. Influenza vaccines had not previously been given; pneumonia vaccines, however, had been given in one school.

In the two hospitals at Kankakee and Jacksonville the candidates were selected from alphabetic lists. A certain number of patients showing signs of illness, including those having tuberculosis, were not considered suitable for observation. All the other inmates were listed alphabetically by wards. The subjects for vaccination were taken from these lists alternately, so far as the mental conditions of the patients permitted. Since the medical officers in charge thought the vaccine treatment undesirable in the management of some cases, certain objects, whom it seemed unwise to coerce, were shifted to the unvaccinated side of the list. The number of such cases was comparatively small, and, as their objection consisted simply in unwillingness to have the hypodermic needle used, this shifting of cases did not affect materially the principle of arbitrary selection. It was unnecessary to discriminate in respect to seriously ill patients, as these had not been listed for observation and do not appear in either the "vaccinated" or "unvac-

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inated" group. The ordinary fluctuations in the respiratory condition of the patients was not considered in the selection of subjects for vaccination.

The patients selected by the method of alphabetic alteration were brought in groups to the vaccinating staffs. They were successively inoculated by the institutions' physicians, and their names were then checked on the lists. At this point the schedule again received slight alterations, since some of the patients selected for vaccination could not be found at the time and were shifted to the unvaccinated group. In addition, there were a few minor oversights and misunderstandings, and in one or two wards the selections, while arbitrary, had not been in alternation from the lists.

A few patients who received the first dose but failed to appear for the second or for the third were dropped from the list altogether and are not included in the tables.

The result of all these minor changes is that the vaccinated group is somewhat smaller than the unvaccinated group, and the distribution of vaccinated cases, while mainly in accord with our original schedule, is not entirely so. It may, however, be stated that choice of the groups finally prepared for observation and comparison had not been influenced by any sort of purposeful selection other than, to some extent, the mental attitude toward injection.

It was not always possible to have in each ward equal numbers of vaccinated and unvaccinated, but the differences were not great. The Kankakee institution, for instance, supplied forty-one ward lists. The ward capacity varied from 15 to above 200 patients, being in very few instances below 30, in nearly half from 30 to 60 and in nearly half from 60 to 140. After all alterations of the lists, thirty-one of the ward lists indicated that in each ward from 46 to 52% of the patients available for comparisons had been vaccinated. Six of the remaining 10 lists showed from 24 to 41% vaccinated, 3 from 55 to 59% and one (with 32 patients) 100%.

In the schools for the blind and for the deaf similar alternate alphabetic selections were made from lists of pupils. In the third school, the University of Chicago, vaccination was optional.

All vaccinations were made with a saline suspension of a standard vaccine prepared under the direction of Dr. W. H. Park of the Influenza Commission in the Research Laboratory of the New York City Health Department. The vaccines were given subcutaneously in three doses at weekly intervals. The first dose contained: the Pfeiffer bacillus, 500

million; *Streptococcus hemolyticus*, 500 million; *Streptococcus viridans*, 500 million; pneumococcus type I, 1,000 million; pneumococcus type II, 1,000 million; pneumococcus type III, 500 million. The second and third doses contained double these numbers of each organism. A few of the smaller children were given only half doses. The injections were made between November 24 and December 11 in 4 of the institutions, and between November 3 and December 16 in the fifth (the University).

The Kankakee and Jacksonville State Hospitals for the Insane included respectively 3,012 and 2,145 cases available for comparison. Practically all were adults. The general condition of these patients was for the most part good. In recent years perhaps a dozen pneumonia cases have developed yearly in each institution. The Kankakee Hospital was touched very lightly by the influenza epidemic of 1918-19. About 12 pneumonia cases developed, hardly more than in normal years. Approximately 100 cases were then diagnosed as influenza, many of these diagnoses doubtless being influenced here as elsewhere by the general prevalence of the disease.

The Jacksonville Hospital, on the other hand, suffered from a pronounced influenza epidemic in the fall of 1918. The Managing Officer's report of Dec. 3, 1918, shows a record of 358 influenza cases, with 17 deaths. This institution was quarantined Oct. 1, 1918; the first cases developed October 16, the largest number October 28 and the last on November 25. None of the patients at that time received a prophylactic vaccine against influenza or pneumonia.

The State Schools for the Deaf and for the Blind, both at Jacksonville, included respectively 355 and 207 cases for comparison, all the patients being children. The School for the Blind escaped the influenza epidemics of 1918-19, but the School for the Deaf had a marked outbreak of influenza during that period. About 150 influenza cases developed in the latter institution, many being complicated by pneumonia. There was one death. Some of the pupils in this school had previously received "antipneumonia" vaccines of unspecified composition.

Approximately 600 students of the University of Chicago volunteered to cooperate in a respiratory disease study. A number of these gave a detailed preliminary report covering history, susceptibility, etc., and followed this up by reports of respiratory disorders as they occurred, with a final report on June 1, 1920. Vaccination was given

to those who desired it. It is evident that grouping according to voluntary application for vaccination is unsatisfactory as compared with arbitrary alternate selection from alphabetic lists, as was done in the other 4 institutions; 164 students received the three vaccine injections and 183 none. Some students that had previously received respiratory vaccines are not included in this summary, nor are any except those whose reports covered the entire period of observation.

Those persons who received only one or two doses of the vaccines are excluded from the series. The figures for the various institutions comprise only persons included in our lists who received either three injections or none.

Reports of all respiratory ailments developing in the University group were made by the students themselves on printed forms, and were supplemented when practicable by the observations of a medical examiner. In the state institutions the respective medical staffs observed, diagnosed and recorded such conditions without respect to the groups involved. These records were sent to us each month, for comparison with our original lists of persons observed.

When the influenza epidemics of January and February, 1920, spread over Illinois, the 5 institutions under observation were all touched. It is interesting to note that so far as could be determined the distribution among these institutions was about proportional with the distribution of the previous epidemics of 1918-1919. The Jacksonville Hospital alone had a considerable number of cases, and it did not suffer heavily.

The city of Jacksonville had 1,000 or so influenza cases. The Jacksonville State Hospital developed 172 and the State Schools for the Deaf and for the Blind 20 and 13, respectively. The symptoms were typical; chilliness at onset, cough, headache and sometimes general aching, a temperature of 101 to 104 degrees, down after 2 days or sometimes irregular for a few days more, etc. Complicating pneumonia was usually of the bronchial type.

While the city of Kankakee had a marked epidemic, patients of the Kankakee State Hospital escaped with 18 cases. The University of Chicago group reported 47. Our figures are somewhat below the total incidence in the institutions by reason of certain exclusions from our lists as elsewhere explained.

Table 1 shows the effect of the prophylactic vaccinations on the development of influenza. The total number of observed persons is

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seen to be 47.4% vaccinated and 52.6% not vaccinated. Of the vaccinated groups 118 (4.1%) contracted influenza, 7 (5.9%) of whom developed pneumonia, with two deaths. Of the unvaccinated groups, 152 (4.8%) contracted influenza, 12 (7.9%) of whom developed pneumonia, with two deaths. These figures do not indicate that any considerable degree of immunity is conferred by the vaccine; the number of cases is too small to warrant attaching much importance to the slight difference observed. No one age group is better protected than another. This is likewise true of the other pneumonia findings to be presented.

TABLE 1
COMPARISON OF INFLUENZA AND INFLUENZAL PNEUMONIA RATES AMONG THE VACCINATED AND THE UNVACCINATED

Age Group	Vaccinated						Not Vaccinated					
	Influenza Cases					Pneumonia Complications, All Five Institutions	Influenza Cases					Pneumonia Complications, All Five Institutions
	Kan-kakee	Jacksonville	Deaf School	Blind School	Chicago		Kan-kakee	Jacksonville	Deaf School	Blind School	Chicago	
5-10	0	0	4	0	0	0	0	0	0	0	0	0
11-15	0	0	3	3	0	0	0	1	5	2	0	0
16-20	0	1	2	3	3	0	0	1	3	1	12	3
21-25	1	3	0	2	12	0	1	4	0	1	9	0
26-30	0	6	0	1	1	1	0	8	0	0	3	0
31-35	0	4	0	0	3	0	3	4	0	0	1	0
36-40	0	11	0	0	1	1	2	18	0	0	0	3
41-45	1	6	0	0	1	0	0	10	0	0	0	1†
46-50	0	9	0	0	0	0	0	20	0	0	0	3†
51-55	3	9	0	0	0	3†	2	5	0	0	0	0
56-60	1	6	0	0	0	0	2	11	0	0	0	1
61-65	1	5	0	0	0	0	0	10	0	0	0	0
66-70	0	5	0	0	0	0	0	6	0	0	0	1
Over 70	0	5	0	0	0	1†	0	3	0	0	1	0
Unk'wn	0	0	2	0	0	1	1	0	1	0	1	0
Totals	7	70	11	9	21		11	101	9	4	27	
Total influenza.....	118						152					
Pneumonia complications.....						7†						12†

	Total Number Under Observation*	
	Vaccinated	Not Vaccinated
Kankakee.....	1,457	1,555
Jacksonville.....	968	1,177
Deaf School.....	182	173
Blind School.....	102	105
University of Chicago.....	164	183
	2,873	3,193

* The small attack rates seemed not to justify the clerical work of age-grouping all observed persons.

† Of the influenzal pneumonia cases, 4 died, 2 among the vaccinated and 2 among those not vaccinated, 1 in each age group indicated.

It seemed possible that disease incidence or prophylactic reaction might be different among the new arrivals as compared with the old residents. Table 2 enumerates cases selected from table 1 including patients who had been admitted to the residence institutions during the year preceding our inoculations. The influenza incidence is seen to be higher than for the total groups (vaccinated 6.0% and unvaccinated 6.9%) and the pneumonia complications lower (one case unvaccinated), but the proportions between vaccinated and unvaccinated are approximately equal.

TABLE 2
INFLUENZA RATES * AMONG PERSONS ADMITTED WITHIN THE YEAR PRECEDING THE INOCULATIONS

Age Groups	Vaccinated				Not Vaccinated			
	Kanka- kee	Jack- sonville	Deaf School	Blind School	Kanka- kee	Jack- sonville	Deaf School	Blind School
Under 21.....	0	1	2	0	0	1	2	0
21-25.....	1	1	0	1	0	2	0	0
26-30.....	0	3	0	0	0	4	0	0
31-35.....	0	2	0	0	1	0	0	0
36-40.....	0	4	0	0	1	4	0	0
41-45.....	1	1	0	0	0	3	0	0
46-50.....	0	4	0	0	0	5	0	0
51-55.....	0	0	0	0	1	1	0	0
56-60.....	1	2	0	0	1	3*	0	0
Over 60.....	0	1	0	0	0	3	0	0
Influenza totals.....	3	19	2	1	4	26	2	0
Total observed.....	215	151	40	10	265	171	11	16
Grand totals.....	25 cases among 416 persons observed				32 cases among 463 persons observed			

* Of this series, but one case (age 56 and not vaccinated) developed a complicating pneumonia.

Small numbers are particularly unreliable for conclusions on influenza because diagnosis is so largely influenced by epidemic conditions. The Jacksonville Hospital, which suffered the disease in epidemic proportions, might presumably give a truer index than the 5 institutions combined. In that institution the vaccinated patients had an influenza incidence of 7.3%, the unvaccinated 8.6%, proportions not unlike the totals already given.

The observed pneumonia cases not associated with influenza are likewise few in number. Practically all of them occurred in the hospitals at Kankakee and Jacksonville. Nineteen cases developed in these institutions, 6 among the vaccinated and 13 among the unvaccinated. Twelve lobar pneumonia cases occurred, 5 with 3 deaths among the vaccinated and 7 with 4 deaths among the unvaccinated. Tuberculous

pneumonias are not listed. Of cases reported as bronchopneumonia (not during the influenza epidemic) or as pneumonia, type unspecified, there were among the vaccinated 1 and among the unvaccinated 6, with 2 deaths. These proportions, although the actual numbers are small, suggest some degree of immunity to pneumonia due to vaccination. It may be noted that the balance in favor of pneumonia prevention is from the Jacksonville list, the Kankakee cases being about equally divided.

It seemed worth while to determine whether the vaccines used protected against attacks of ordinary colds. The three schools with 909 controlled patients give some information on this point. The greater part of the reports received do not differentiate between various types of colds sufficiently to allow any but collective grouping of such conditions.

Table 3 shows that the vaccinated group, although slightly smaller, reported a somewhat greater total number of colds, and of persons affected with colds than the unvaccinated. This may be misleading, since those who are voluntarily vaccinated are quite likely to be more inclined to notice and report colds carefully. Age groups up to 30 years are included. The figures indicate that such vaccines do not influence in any noteworthy degree susceptibility to ordinary colds.

The proportion of colds reported from the two hospitals was very small, as might be expected from the difficulty of observing such minor ailments among persons with mental diseases. There were reported from the Kankakee and Jacksonville Hospitals, respectively, 135 and 32 colds among the vaccinated and 112 and 17 among the unvaccinated.

Only the University reports are such as to differentiate reliably nose from chest colds. Table 4 shows that the vaccinated group of 164 developed 248 rhinitis attacks, 26 bronchitis and 44 of rhinitis and bronchitis combined, while the unvaccinated 183 developed 216 rhinitis, 25 bronchitis and 28 combined attacks. These figures indicate that no greater protection is obtained against either variety of cold than against the collective average.

As suggested in the foregoing, the voluntary choice of vaccination by the University students admits a possible error. The more susceptible might desire and the less susceptible might be less desirous of prophylactic inoculations. We therefore attempted to determine whether the yearly average of colds in either group was altered following the injections. At the beginning of the observational period, each

TABLE 3
RATE OF ORDINARY "COLDS" AMONG VACCINATED AND UNVACCINATED GROUPS

Age Groups	Vaccinated						Not Vaccinated								
	Persons Under Obser- vation			Persons Contracting Colds			Persons Under Obser- vation			Persons Contracting Colds					
	Chi- cago	Deaf School	Blind School	Chi- cago	Deaf School	Blind School	Chi- cago	Deaf School	Blind School	Chi- cago	Deaf School	Blind School			
5-10.....	0	55	21	0	30	5	0	31	21	0	17	2	0	30	2
11-15.....	0	83	37	0	30	4	2	74	42	1	32	5	1	57	6
16-20.....	45	16	39	43	14	7	99	64	22	78	21	4	138	28	4
21-25.....	90	3	8	81	2	2	162	3	13	41	0	2	77	0	3
26-30.....	17	0	2	17	0	0	30	0	7	20	0	1	34	0	2
Over 30 or unknown.....	12	9	0	11	0	0	27	0	1	16	0	0	19	0	0
Totals.....	164	182	102	152	76	18	318	122	105	154	70	14	269	115	17
Under observation.....	448			246			461			238			401		
Contracted colds.....		
Number of colds.....		

student recorded the average number of colds suffered yearly. Later, reports were obtained showing how many colds developed during this period. The latter reports cover the more prolific respiratory disease months but not an entire year; we might therefore expect fewer colds than the yearly average. Of the vaccinated (table 5), 73 had their usual yearly average of colds, 39 had more and 52 less. Of the unvaccinated, 77 had their usual yearly average, 44 more and 62 less. These figures, showing that the vaccinated persons experienced no greater reduction in the liability to colds than the unvaccinated, largely discount the possibility of error just mentioned.

TABLE 4
ATTACK RATES OF RHINITIS, BRONCHITIS AND THESE COMBINED
(University of Chicago)

Age Groups	Attacks Among the Vaccinated, of			Attacks Among Those Not Vaccinated, of		
	Rhinitis	Bronchitis	Rhinitis and Bronchitis	Rhinitis	Bronchitis	Rhinitis and Bronchitis
11-15.....	0	0	0	0	1	0
16-20.....	73	12	14	113	10	15
21-25.....	135	7	20	62	9	6
26-30.....	22	1	7	30	1	3
Over 30 or unknown.	18	6	3	11	4	4
Totals.....	248	26	44	216	25	28

TABLE 5
FREQUENCY OF COLDS AS AFFECTED BY THE INOCULATIONS
(University of Chicago)

Age Groups	Vaccinated Persons With			Persons Not Vaccinated With		
	More Colds Than Usual	Fewer Than Usual	Usual Number of Colds	More Colds Than Usual	Fewer Than Usual	Usual Number of Colds
11-15.....	0	0	0	1	1	0
16-20.....	11	6	28	20	36	36
21-25.....	21	36	33	14	15	22
26-30.....	3	5	9	5	2	15
Over 30 or unknown.	4	5	3	4	8	4
Totals.....	39	52	73	44	62	77

The reports of other respiratory disorders, tonsillitis, pharyngitis, "sore throat" and laryngitis are too few to warrant any definite conclusions. Both vaccinated and unvaccinated groups, however, reported substantially the same number and kinds of ailments.

An interesting side-light on the subjective reaction to vaccination is furnished by perhaps a dozen unsolicited testimonials. Those vaccinated at the University had been told that possibly colds might be

prevented by vaccination, and toward the end of the period many were kind enough to express their opinion of the result. Two thought the vaccine had done them no good, but most of them optimistically declared that they had received definite benefit in protection against colds. "Satisfied patient" conclusions differ widely from those of controlled statistics.

SUMMARY

The prophylactic effect of a widely used vaccine containing Pfeiffer bacilli, streptococci and pneumococci has been studied clinically and statistically. We have recorded during a period of about 7 months the respiratory ailments which developed among 6,066 persons, approximately half of whom had received the vaccine. Some of these were attacked by influenza in the 1920 wave, which occurred within two months of the vaccination; in addition, the usual number of pneumonia and common cold cases among those observed afford material for comparisons.

Rhinitis and bronchitis developed with frequency about equal in vaccinated and unvaccinated groups.

The influenza attacks among the 2,873 vaccinated numbered 118 (4.1%) and among the 3,193 unvaccinated numbered 152 (4.8%); 7 pneumonia complications with 2 deaths occurred among the 118 vaccinated patients and 12 with 2 deaths in the 152 unvaccinated. Both the influenza and pneumonia attack rates are hence somewhat lower among the vaccinated, but the difference is not great. Pneumonia, not associated with influenza, was also less frequent among the vaccinated, only 6 of 19 pneumonia patients having been vaccinated. The small numbers hardly warrant, although they suggest, a favorable conclusion regarding some slight prophylactic value for pneumonia. That any considerable degree of protection against influenza was conferred by the vaccine seems unlikely.